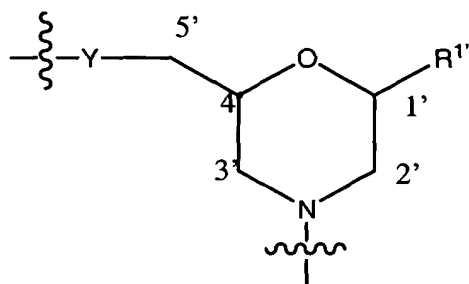


What is Claimed is:

1. A composition comprising a first oligomer and a second oligomer, wherein:
  - at least a portion of said first oligomer is capable of hybridizing with at least a portion of said second oligomer,
  - at least a portion of first oligomer is complementary to and capable of hybridizing to a selected target nucleic acid,
  - at least one of said first or said second oligomers includes at least one nucleotide having a modification comprising a peptide nucleic acid, a peptide nucleic acid mimic, a morpholino nucleic acid, hexose sugar with amide linkage, cyclohexenyl nucleic acid (CeNA) or an acyclic backbone moiety.
2. The composition of claim 1 wherein said first and said second oligomers are a complementary pair of siRNA oligomers.
3. The composition of claim 1 wherein said first and said second oligomers are an antisense/sense pair of oligomers.
4. The composition of claim 1 wherein each of said first and second oligomers has 10 to 40 nucleotides.
5. The composition of claim 1 wherein each of said first and second oligomers has 18 to 30 nucleotides.
6. The oligomer composition of claim 1 wherein each of said first and second oligomers has 21 to 24 nucleotides.
7. The composition of claim 1 wherein said first oligomer is an antisense oligomer.
8. The composition of claim 7 wherein said second oligomer comprises a sense oligomer.
9. The composition of claim 7 wherein said second oligomer has a plurality of ribose nucleotide units.

10. The composition of claim 1 wherein said first oligomer includes said nucleotide having said modification.
11. The composition of claim 1 wherein the modification is a morpholino nucleic acid.
12. The composition of claim 11 wherein the oligomer comprises at least one monomer of the formula:



where

Y is a linking group; and

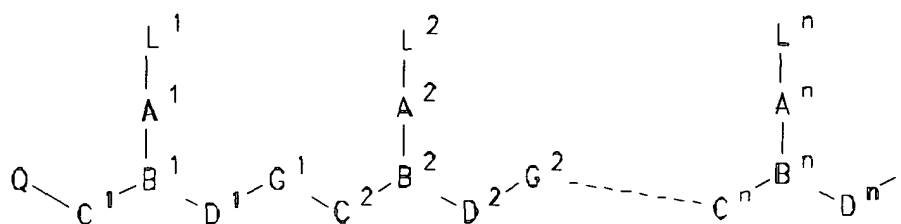
R<sup>1'</sup> is hydrogen, hydroxy, (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, and heterocyclic moieties, reporter ligands.

13. The composition of claim 12 wherein at least one R<sup>1'</sup> is a naturally occurring nucleobases or non-naturally occurring nucleobase.
14. The composition of claim 12 wherein Y is a phosphate, phosphorothioate; phosphorodithioate; phosphonate; phosphonothioate; phosphotriester; phosphorothiotriester; phosphoramidate; phosphorothioamidate; phosphinate; and boronate linkage.
15. The composition of claim 12 wherein Y is an ether-, allyl ether-, allyl sulfide-, formacetal/ketal- sulfide-, sulfoxide-, sulfone-, sulfamate-, sulfonamide-, siloxane-, amide-, cationic alkylpolyamine-, guanidyl-, morpholino-, hexose sugar or amide-containing linkage, or a two to four atom linkage containing C, N, O, or S atoms.

16. The composition of claim 12 wherein Y is -NHC(=O)-O-, -CH<sub>2</sub>CH<sub>2</sub>-O-, -CH<sub>2</sub>C(=O)-NH-, -SO<sub>2</sub>-N(CH<sub>3</sub>)-, N-alkylphoramidite, phosphothioate, or phosphate.

17. The composition of claim 1 wherein the modification is a peptide nucleic acid.

18. The composition of claim 17 wherein the peptide nucleic acid is of the formula:

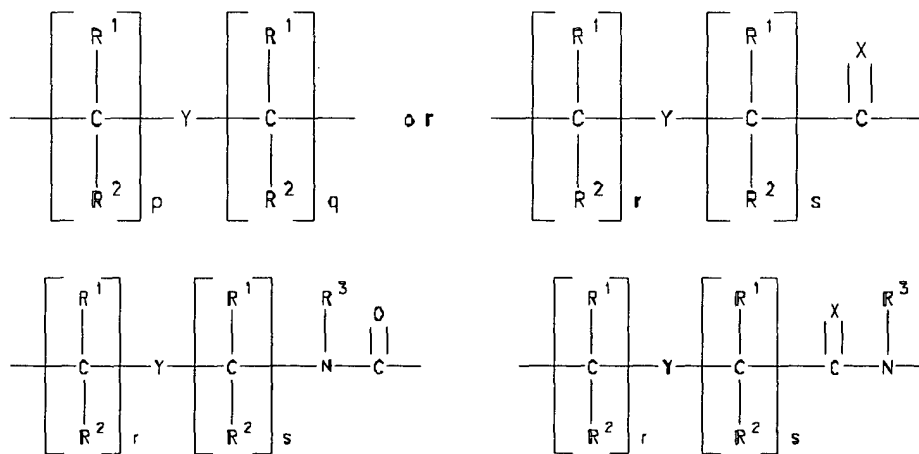


wherein:

n is at least 2,

each of L<sup>1</sup>-L<sup>n</sup> is independently selected from the group consisting of hydrogen, hydroxy, (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, heterocyclic moieties, and reporter ligands, at least one of L<sup>1</sup>-L<sup>n</sup> being a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

each of A<sup>1</sup>-A<sup>n</sup> is a single bond, a methylene group or a group of formula:



where:

X is O, S, Se,  $\text{NR}^3$ ,  $\text{CH}_2$  or  $\text{C}(\text{CH}_3)_2$ ;

Y is a single bond, O, S or  $\text{NR}^4$ ;

each of p and q is zero or an integer from 1 to 5, the sum  $p + q$  being not more than 10;

each of r and s is zero or an integer from 1 to 5, the sum  $r + s$  being not more than 10;

each  $\text{R}^1$  and  $\text{R}^2$  is independently selected from the group consisting of hydrogen,  $(\text{C}_1\text{-C}_4)$ alkyl which may be hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen; and

each  $\text{R}^3$  and  $\text{R}^4$  is independently selected from the group consisting of hydrogen,  $(\text{C}_1\text{-C}_4)$ alkyl, hydroxy- or alkoxy- or alkylthio-substituted  $(\text{C}_1\text{-C}_4)$ alkyl, hydroxy, alkoxy, alkylthio and amino;

each of  $\text{B}^1\text{-B}^n$  is N or  $\text{R}^3\text{N}^+$ , where  $\text{R}^3$  is as defined above;

each of  $\text{C}^1\text{-C}^n$  is  $\text{CR}^6\text{R}^7$ ,  $\text{CHR}^6\text{CHR}^7$  or  $\text{CR}^6\text{R}^7\text{CH}_2$ , where  $\text{R}^6$  is hydrogen and  $\text{R}^7$  is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or  $\text{R}^6$  and  $\text{R}^7$  are independently selected from the group consisting of hydrogen,  $(\text{C}_2\text{-C}_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy,  $(\text{C}_1\text{-C}_6)$ alkoxy,  $(\text{C}_1\text{-C}_6)$ alkylthio,  $\text{NR}^3\text{R}^4$  and  $\text{SR}^5$ , where  $\text{R}^3$  and  $\text{R}^4$  are as defined above, and  $\text{R}^5$  is hydrogen,  $(\text{C}_1\text{-C}_6)$ alkyl, hydroxy-, alkoxy-, or alkylthio-substituted  $(\text{C}_1\text{-C}_6)$ alkyl, or  $\text{R}^6$  and  $\text{R}^7$  taken together complete an alicyclic or heterocyclic system;

each of  $\text{D}^1\text{-D}^n$  is  $\text{CR}^6\text{R}^7$ ,  $\text{CH}_2\text{CR}^6\text{R}^7$  or  $\text{CHR}^6\text{CHR}^7$ , where  $\text{R}^6$  and  $\text{R}^7$  are as defined above;

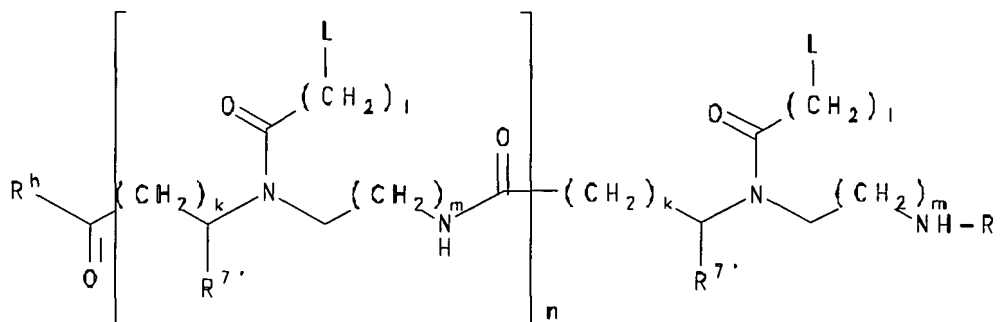
each of  $\text{G}^1\text{-G}^{n-1}$  is  $-\text{NR}^3\text{CO}-$ ,  $-\text{NR}^3\text{CS}-$ ,  $-\text{NR}^3\text{SO}-$  or  $-\text{NR}^3\text{SO}^2-$ , in either orientation, where  $\text{R}^3$  is as defined above;

Q is  $-\text{CO}_2\text{H}$ ,  $-\text{CONR}^3\text{R}^4$ ,  $-\text{SO}_3\text{H}$  or  $-\text{SO}_2\text{NR}^3\text{R}^4$  or an activated derivative of  $-\text{CO}_2\text{H}$  or  $-\text{SO}_3\text{H}$ ; and

I is  $-\text{NHR}^1\text{R}^2$  or  $-\text{NR}^1\text{C}(\text{O})\text{R}^2$ , where  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$  and  $\text{R}^4$  are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligomers and soluble and non-soluble polymers.

19. The composition of claim 17 wherein the peptide nucleic acid is of the

formula:



wherein:

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic moieties, naturally occurring nucleobases, and non-naturally occurring nucleobases;

each R<sup>7'</sup> is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

$n$  is an integer from 1 to 60,

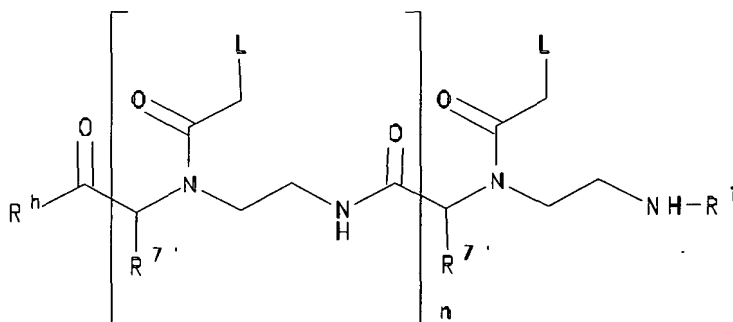
each  $k$  and  $m$  is, independently, zero or 1;

each  $l$  is zero or an integer from 1 to 5;

R<sup>h</sup> is OH, NH<sub>2</sub> or -NHLysNH<sub>2</sub>; and

$R^i$  is H or  $COCH_3$ .

20. The composition of claim 17 wherein the peptide nucleic acid is of the formula:

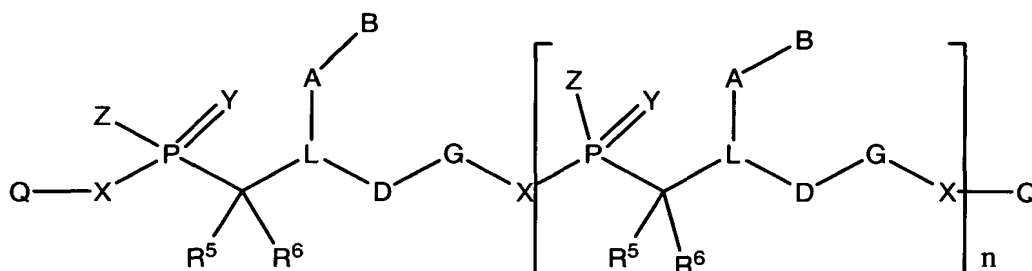


each L is independently selected from the group consisting of the nucleobases

each R<sup>7'</sup> is hydrogen; and

n is an integer from 1 to 30.

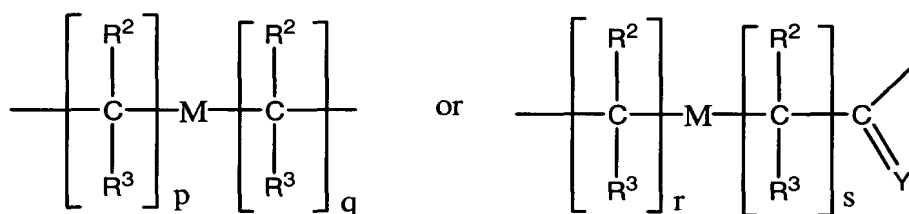
21. The composition of claim 20 wherein n is from 20 to about 23.
22. The composition of claim 17 wherein the peptide nucleic acid is of the formula:



wherein:

n is a number from zero to 100;

A independently of one another is a single bond, a methylene group or a group of formula



in which M is a single bond, --O--, --S-- or --NR<sup>1</sup> --, where R<sup>1</sup> is hydrogen or (C<sub>1</sub> - C<sub>6</sub>)-alkyl optionally substituted by hydroxyl, (C<sub>1</sub> - C<sub>6</sub>)-alkoxy, (C<sub>1</sub> - C<sub>6</sub>)-alkylthio or amino;

R<sup>2</sup> and R<sup>3</sup> independently of one another are hydrogen, hydroxyl, (C<sub>1</sub> - C<sub>6</sub>)-alkoxy, (C<sub>1</sub> - C<sub>6</sub>)-alkylthio, amino, halogen, or (C<sub>1</sub> - C<sub>6</sub>)-alkyl optionally substituted by hydroxyl, (C<sub>1</sub> - C<sub>6</sub>)-alkoxy or (C<sub>1</sub> - C<sub>6</sub>)-alkylthio;

p and q independently of one another are zero to 5; and

r and s independently of one another are zero to 5;

B independently of one another is hydrogen, hydroxyl, (C<sub>1</sub> - C<sub>20</sub>)-alkyl, (C<sub>1</sub> - C<sub>20</sub>)-alkoxy, (C<sub>1</sub> - C<sub>20</sub>)-alkylthio, (C<sub>6</sub> - C<sub>20</sub>)-aryl-(C<sub>1</sub> - C<sub>6</sub>)-alkyl, (C<sub>6</sub> - C<sub>20</sub>)-aryl-(C<sub>1</sub> - C<sub>6</sub>)-alkoxy, (C<sub>6</sub> - C<sub>20</sub>)-aryl-(C<sub>1</sub> - C<sub>6</sub>)-alkylthio, an aromatic group or a heterocyclic group, wherein the alkyl, alkyl portion of alkoxy or alkylthio, aromatic or heterocyclic group is optionally substituted one or more times by hydroxyl, (C<sub>1</sub> -

C<sub>4</sub>)-alkoxy, --NR<sup>9</sup>R<sup>10</sup>, oxo, --C(O)OR<sup>8</sup>, --C(O)NR<sup>9</sup>R<sup>10</sup>, --CN, --F, --Cl, --Br, --NO<sub>2</sub>, (C<sub>2</sub>-C<sub>6</sub>)-alkoxyalkyl, --S(O)<sub>m</sub>R<sup>8</sup>, --(C<sub>1</sub>-C<sub>6</sub>)-alkyl--S(O)<sub>m</sub>R<sup>8</sup>, --NHC(=NH)NHR<sup>8</sup>, --C(=NH)NHR<sup>9</sup>, NR<sup>9</sup>C(=O)R<sup>8</sup>, =NOR<sup>8</sup>, NR<sup>9</sup>C(=O)OR<sup>10</sup>, --OC(=O)NR<sup>9</sup>R<sup>10</sup>, --NR<sup>9</sup>C(=O)NR<sup>9</sup>R<sup>10</sup>, a natural nucleobase, an unnatural nucleobase or a reporter ligand, with the proviso that at least one B moiety is a nucleobase;

m is zero, 1 or 2; or,

A-B independent of other A and B groups, can be a D- or L-amino acid condensed on via the carboxyl group or a peptide containing amino acids having a length of up to 5 amino acid residues, with the proviso that at least one B moiety is a nucleobase;

L independently of one another is N or R<sup>1</sup>N<sup>+</sup>, where R<sup>1</sup> is as defined above; and

Y' is =O, =S, =CH<sub>2</sub>, =C(CH<sub>3</sub>)<sub>2</sub> or =NR<sup>1</sup>, where R<sup>1</sup> is as defined above;

D and G each independently represent CR<sup>5</sup>R<sup>6</sup> which can be the same or different;

R<sup>5</sup> and R<sup>6</sup> independently of one another are hydrogen, (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>6</sub>-C<sub>20</sub>)-aryl, (C<sub>6</sub>-C<sub>20</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, hydroxyl, (C<sub>1</sub>-C<sub>6</sub>)-alkoxy, (C<sub>1</sub>-C<sub>6</sub>)-alkylthio, wherein the alkyl, alkyl portion of alkoxy or alkylthio, or aryl group is optionally substituted by SR<sup>1</sup> or NR<sup>1</sup>R<sup>1</sup>, where R<sup>1</sup> is as defined above and R<sup>1</sup> independently of R<sup>1</sup> has the same meaning as R<sup>1</sup>;

X independently of one another is --O--, --S-- or --NR<sup>1</sup>--, in which R<sup>1</sup> is as defined above;

Y independently of one another is =O or =S;

Z independently of one another is --OR<sup>8</sup>, --NR<sup>9</sup>R<sup>10</sup> or X'Q", where X' is defined as X above and Q" is defined as Q below;

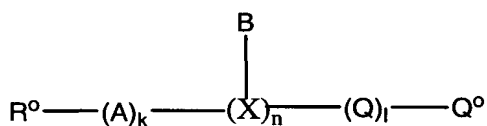
R<sup>8</sup> is hydrogen, (C<sub>1</sub>-C<sub>18</sub>)-alkyl, (C<sub>2</sub>-C<sub>18</sub>)-alkenyl, (C<sub>3</sub>-C<sub>18</sub>)-alkynyl, (C<sub>6</sub>-C<sub>12</sub>)-aryl, (C<sub>6</sub>-C<sub>12</sub>)-aryl-(C<sub>1</sub>-C<sub>6</sub>)-alkyl, wherein alkyl is optionally substituted one or more times by hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy, F, Cl or Br and wherein aryl is optionally substituted 1-3 times by hydroxyl, (C<sub>1</sub>-C<sub>4</sub>)-alkoxy, (C<sub>1</sub>-C<sub>4</sub>)-alkyl, F, Cl, Br, NO<sub>2</sub>, --NR<sup>9</sup>R<sup>10</sup>, --C(O)OH, --C(O)O--(C<sub>1</sub>-C<sub>6</sub>)-alkyl or --C(O)NR<sup>9</sup>R<sup>10</sup>;

R<sup>9</sup> and R<sup>10</sup> independently of one another are hydrogen, (C<sub>1</sub>-C<sub>18</sub>)-alkyl, (C<sub>2</sub>

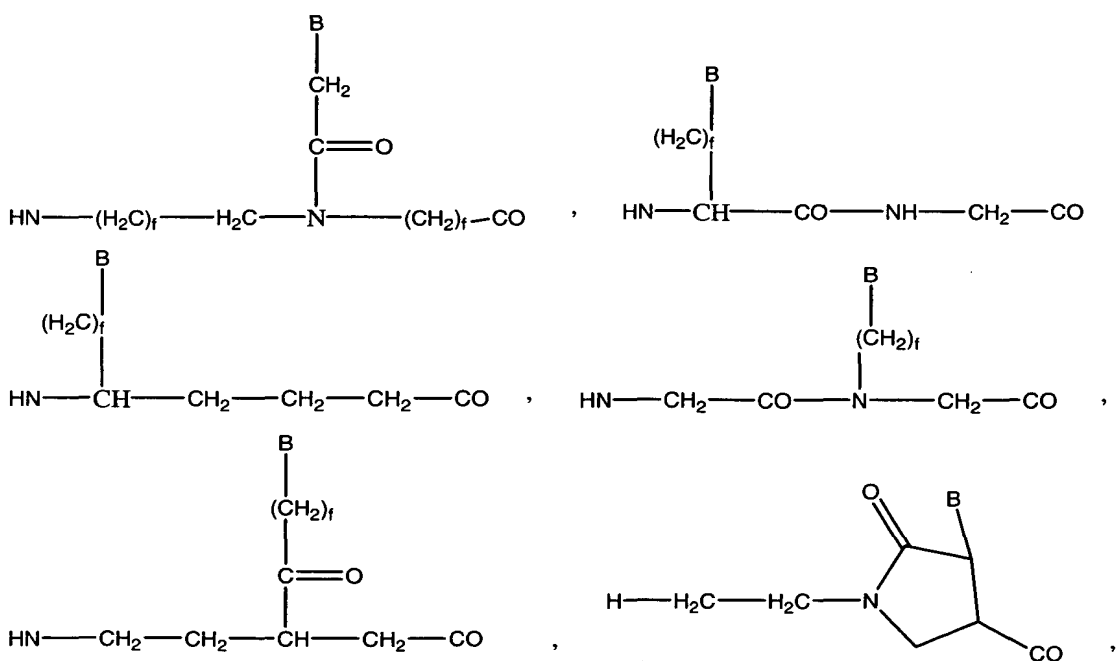
$-(C_{18})$ -alkenyl,  $(C_3-C_{18})$ -alkynyl,  $(C_6-C_{12})$ -aryl,  $(C_6-C_{12})$ -aryl- $(C_1-C_6)$ -alkyl, where alkyl is optionally substituted one or more times by hydroxyl,  $(C_1-C_4)$ -alkoxy, F, Cl or Br; or  $R^9$  and  $R^{10}$  form a 4 to 7-membered ring together with the N atom in  $--NR^9R^{10}$ ;

Q and Q' independently of one another are  $R^8$ , modified or unmodified oligonucleotides or conjugates which a) favorably affect the properties of antisense oligonucleotides, b) affect the properties of triple helix-forming oligonucleotides, c) serve as a label of a DNA probe, or d) during the hybridization of the oligonucleotide analog to the target nucleic acid, attack the target nucleic acid with binding or cross-linking; or Q and Q' alone or together are a single bond in a cyclic molecule; or Q and Q', when neither is hydrogen, can be linked together to form a cyclic molecule.

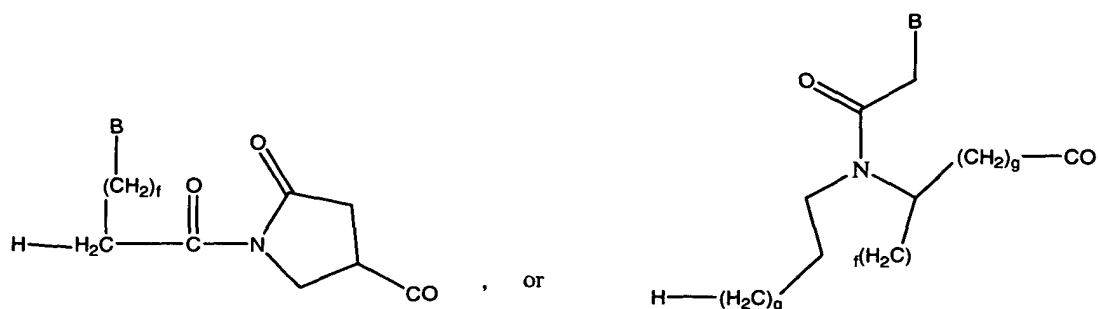
23. The composition of claim 17 wherein the peptide nucleic acid is of the formula:



in which B-X is







where  $f$  is 1-4 and  $g$  is 0-3;  $R^0$  is hydrogen,  $C_1$ - $C_{18}$ -alkanoyl,  $C_1$ - $C_{18}$ -alkoxy-carbonyl,  $C_3$ - $C_8$ -cycloalkanoyl,  $C_7$ - $C_{15}$ -aroyl,  $C_3$ - $C_{13}$ -heteroaroyl, or a group which favors intracellular uptake of the oligomer;

A is an amino acid radical;

$k$  is an integer from zero to 10;

Q is an amino acid radical;

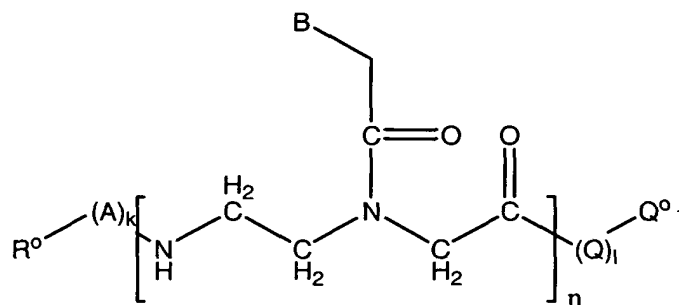
$l$  is an integer from zero to 10;

B is a natural nucleotide base or unnatural nucleotide base conventionally used in nucleotide chemistry or their prodrug forms, or a base substitute compound;

$Q^0$  is hydroxyl,  $NH_2$  or  $NHR''$ , in which  $R''$  is  $C_1$ - $C_{18}$ -alkyl,  $C_2$ - $C_{18}$ -aminoalkyl or  $C_2$ - $C_{18}$ -hydroxyalkyl; and

$n$  is an integer from 1-50.

24. The composition of claim 17 wherein the peptide nucleic acid is of the formula:



wherein:

$R^0$  is hydrogen,  $C_1$ - $C_{18}$ -alkanoyl,  $C_1$ - $C_{18}$ -alkoxycarbonyl,  $C_3$ - $C_8$ -cycloalkanoyl,  $C_7$ - $C_{15}$ -aroyl,  $C_3$ - $C_{13}$ -heteroaroyl, or a group which favors

intracellular uptake of the oligomer;

A is an amino acid residue;

k is an integer from zero to 10;

Q is an amino acid residue;

m is an integer from 0 to 20;

B is a nucleotide base;

$Q^o$  is hydroxyl,  $NH_2$  or  $NHR''$ , with  $R''$  is  $C_1-C_{18}$ -alkyl,  $C_2-C_{18}$ -aminoalkyl or  $C_2-C_{18}$ -hydroxyalkyl; and

n is an integer of 1-50.

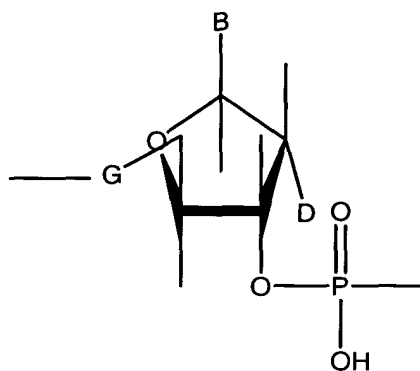
25. The composition of claim 17 wherein the peptide nucleic acid is of the formula:



wherein

Q is a linker or chemical bond;

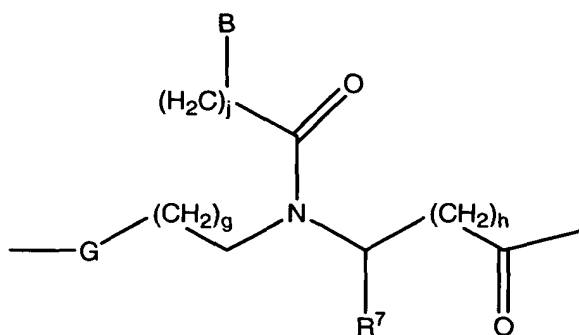
one of L and M is a nucleotide moiety of the formula:



where B is a natural or unnatural nucleobase comprising a bond linking a nucleobase protecting group to the natural or unnatural nucleobase; and

D is a hydrogen atom, a hydroxyl group, a methoxyl group or a hydroxyl group which is protected by a protecting group;

the other of L and M is a PNA moiety of the formula:



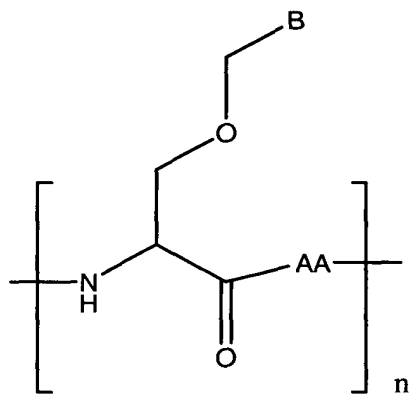
wherein G is a secondary nitrogen atom, a tertiary nitrogen atom having an alkyl substituent, an oxygen atom or a sulfur atom;

B is a natural or unnatural nucleobase;

$R^7$  is selected from the group consisting of hydrogen and a side chain of a protected or unprotected naturally occurring  $\alpha$ -amino acid; and

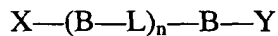
each of j, g and h is the same or different and is independently zero or an integer from one to five.

26. The composition of claim 17 wherein the peptide nucleic acid is of the formula:



where B is a nucleobase, AA is an amino acid, and n is an integer greater than 1.

27. The composition of claim 1 wherein the modification is of the formula:



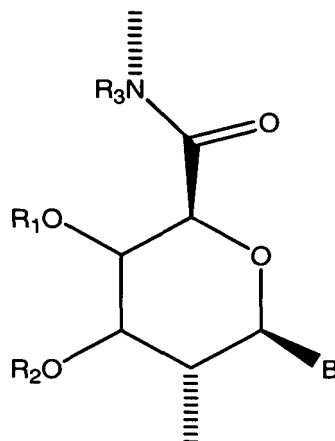
where B is a nucleobase capable of effecting Watson/Crick base-pairing and bearing two linking attachment sites;

L is a linker comprising 4-7 bonds;

X and Y are terminating groups; and

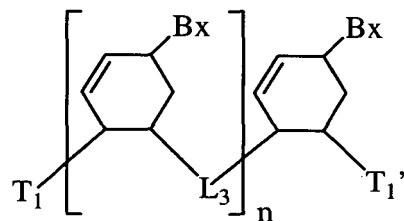
n is an integer equal to 1 or greater.

28. The composition of claim 1 wherein the modification is of formula:



wherein  $R_1$  and  $R_2$  are, independently, hydrogen, lower alkyl or acyl and  $R_3$  is hydrogen or lower alkyl.

29. The composition of claim 1 wherein the modification is of the formula:



wherein

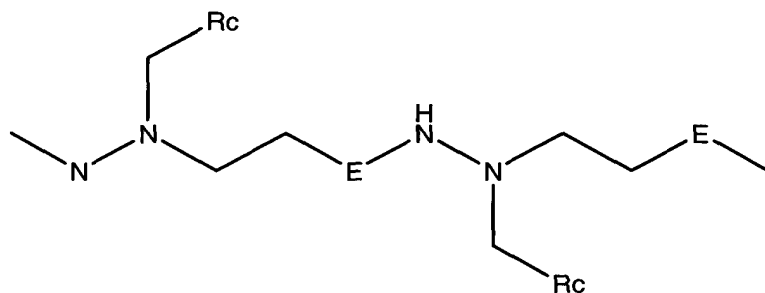
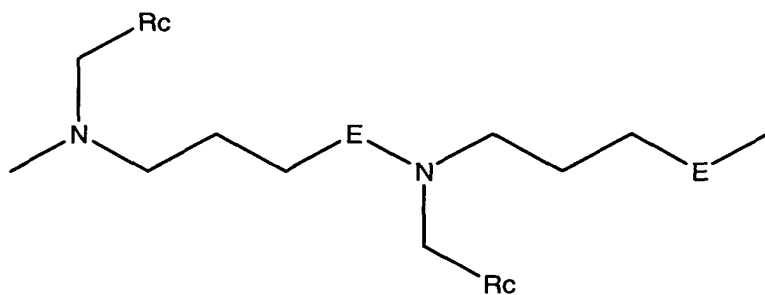
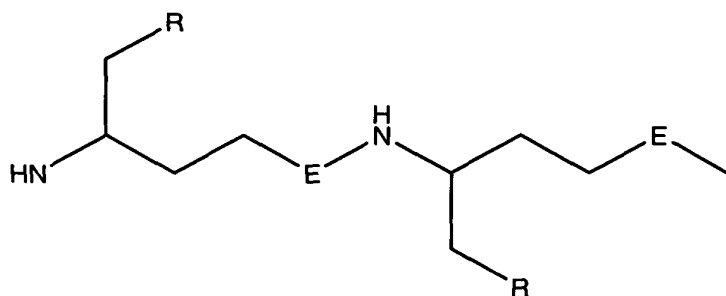
each  $Bx$  is a heterocyclic base moiety;

$T_1$  is hydroxyl or a protected hydroxyl;

$T_1'$  is hydroxyl or a protected hydroxyl; and

$L_3$  is an internucleoside linkage.

31. The composition of claim 1 wherein the modification is of the formula:



where E is C(=O) or SO<sub>2</sub>; and

R and Rc are each independently selected from the group consisting of hydrogen, hydroxy, (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, heterocyclic moieties, and reporter ligands, at least one of R and Rc being a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group.

30. The composition of claim 29 wherein at least one R or Rc is a naturally occurring nucleobase, a non-naturally occurring nucleobase.

32. A composition comprising an oligomer complementary to and capable of

hybridizing to a selected target nucleic acid and at least one protein, said protein comprising at least a portion of a RNA-induced silencing complex (RISC), wherein:

said oligomer includes at least one nucleotide having a modification comprising a peptide nucleic acid, a peptide nucleic acid mimic, a morpholino nucleic acid, hexose sugar with amide linkage, cyclohexenyl nucleic acid (CeNA) or an acyclic backbone moiety.

33. The composition of claim 32 wherein said oligomer is an antisense oligomer.

34. The composition of claim 32 wherein said oligomer has 10 to 40 nucleotides.

35. The composition of claim 32 wherein said oligomer has 18 to 30 nucleotides.

36. The composition of claim 32 wherein said oligomer has 21 to 24 nucleotides.

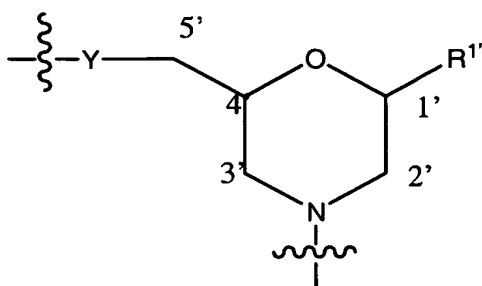
37. The composition of claim 32 further including a further oligomer, wherein said further oligomer is complementary to said oligomer.

38. The composition of claim 37 wherein said further oligomer is a sense oligomer.

39. The composition of claim 37 wherein said further oligomer is an oligomer having a plurality of ribose nucleotide units.

40. The composition of claim 32 wherein the modification is a morpholino nucleic acid.

41. The composition of claim 40 wherein the oligomer comprises at least one monomer of the formula:



where

Y is a linking group; and

R<sup>1'</sup> is hydrogen, hydroxy, (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, and heterocyclic moieties, reporter ligands.

42. The composition of claim 41 wherein at least one R<sup>1'</sup> is a naturally occurring nucleobases or non-naturally occurring nucleobase.

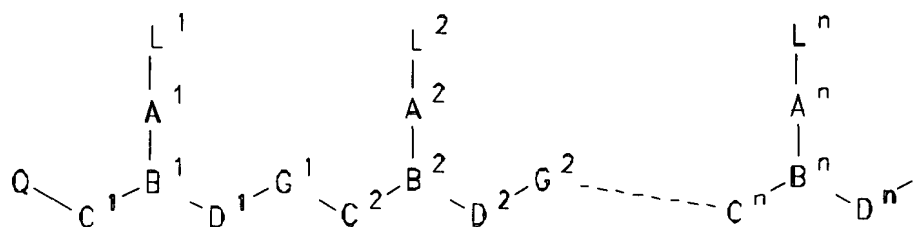
43. The composition of claim 41 wherein Y is a phosphate, phosphorothioate; phosphorodithioate; phosphonate; phosphonothioate; phosphotriester; phosphorothiotriester; phosphoramidate; phosphorothioamidate; phosphinate; and boronate linkage.

44. The composition of claim 41 wherein Y is an ether-, allyl ether-, allyl sulfide-, formacetal/ketal- sulfide-, sulfoxide-, sulfone-, sulfamate-, sulfonamide-, siloxane-, amide-, cationic alkylpolyamine-, guanidyl-, morpholino-, hexose sugar or amide-containing linkage, or a two to four atom linkage containing C, N, O, or S atoms.

45. The composition of claim 41 wherein Y is -NHC(=O)-O-, -CH<sub>2</sub>CH<sub>2</sub>-O-, -CH<sub>2</sub>C(=O)-NH-, -SO<sub>2</sub>-N(CH<sub>3</sub>)-, N-alkylphoramidite, phosphothioate, or phosphate.

46. The composition of claim 32 wherein the modification is a peptide nucleic acid.

47. The composition of claim 46 the peptide nucleic acid is of the formula:

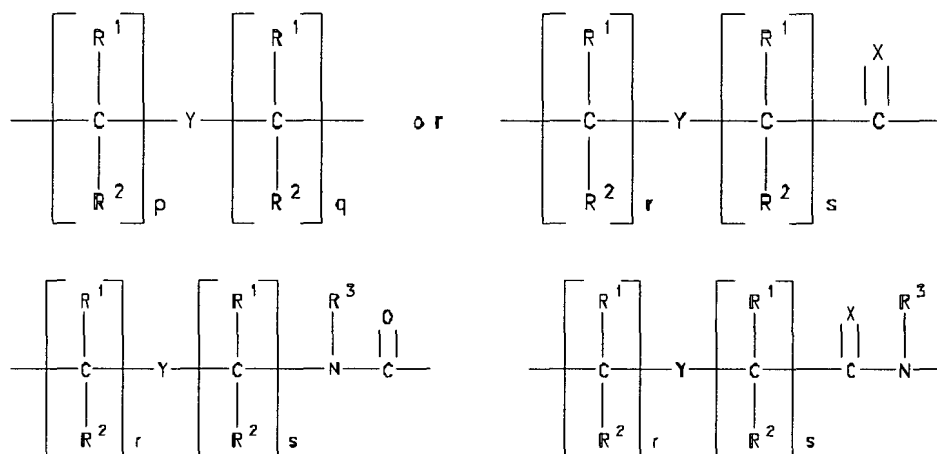


wherein:

$n$  is at least 2,

each of  $L^1$ - $L^n$  is independently selected from the group consisting of hydrogen, hydroxy,  $(C_1-C_4)$ alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, heterocyclic moieties, and reporter ligands, at least one of  $L^1$ - $L^n$  being a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

each of  $A^1$ - $A^n$  is a single bond, a methylene group or a group of formula:



where:

$X$  is O, S, Se,  $NR^3$ ,  $CH_2$  or  $C(CH_3)_2$ ;

$Y$  is a single bond, O, S or  $NR^4$ ;

each of  $p$  and  $q$  is zero or an integer from 1 to 5, the sum  $p + q$  being not more than 10;

each of  $r$  and  $s$  is zero or an integer from 1 to 5, the sum  $r + s$  being not more than 10;

each  $R^1$  and  $R^2$  is independently selected from the group consisting of hydrogen,  $(C_1-C_4)$ alkyl which may be hydroxy- or alkoxy- or alkylthio-



substituted, hydroxy, alkoxy, alkylthio, amino and halogen; and

each  $R^3$  and  $R^4$  is independently selected from the group consisting of hydrogen, (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C<sub>1</sub>-C<sub>4</sub>)alkyl, hydroxy, alkoxy, alkylthio and amino;

each of  $B^1$ - $B^n$  is N or  $R^3N^+$ , where  $R^3$  is as defined above;

each of  $C^1$ - $C^n$  is  $CR^6R^7$ ,  $CHR^6CHR^7$  or  $CR^6R^7CH_2$ , where  $R^6$  is hydrogen and  $R^7$  is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or  $R^6$  and  $R^7$  are independently selected from the group consisting of hydrogen, (C<sub>2</sub>-C<sub>6</sub>)alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)alkylthio,  $NR^3R^4$  and  $SR^5$ , where  $R^3$  and  $R^4$  are as defined above, and  $R^5$  is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C<sub>1</sub>-C<sub>6</sub>)alkyl, or  $R^6$  and  $R^7$  taken together complete an alicyclic or heterocyclic system;

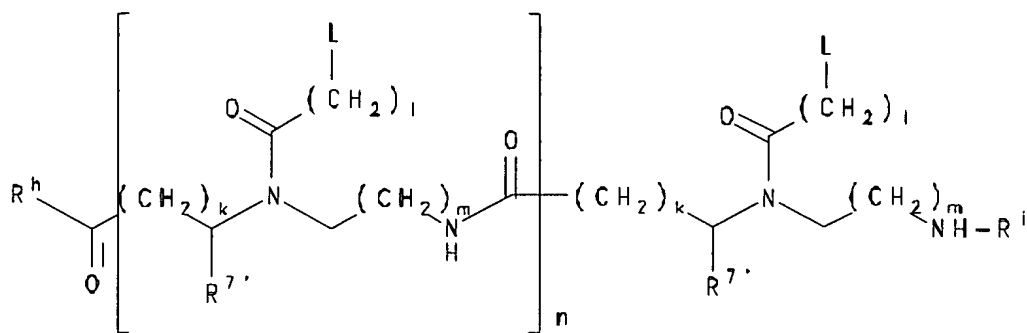
each of  $D^1$ - $D^n$  is  $CR^6R^7$ ,  $CH_2CR^6R^7$  or  $CHR^6CHR^7$ , where  $R^6$  and  $R^7$  are as defined above;

each of  $G^1$ - $G^{n-1}$  is  $-NR^3CO-$ ,  $-NR^3CS-$ ,  $-NR^3SO-$  or  $-NR^3SO^{2-}$ , in either orientation, where  $R^3$  is as defined above;

Q is  $-CO_2H$ ,  $-CONR^3R''$ ,  $-SO_3H$  or  $-SO_2NR^3R''$  or an activated derivative of  $-CO_2H$  or  $-SO_3H$ ; and

I is  $-NHR^3R^4R^5$  or  $-NR^3C(O)R^4R^5$ , where  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides and soluble and non-soluble polymers.

48. The composition of claim 46 wherein the peptide nucleic acid is of the formula:



wherein:

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic moieties, naturally occurring nucleobases, and non-naturally occurring nucleobases;

each R<sup>7'</sup> is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

n is an integer from 1 to 60,

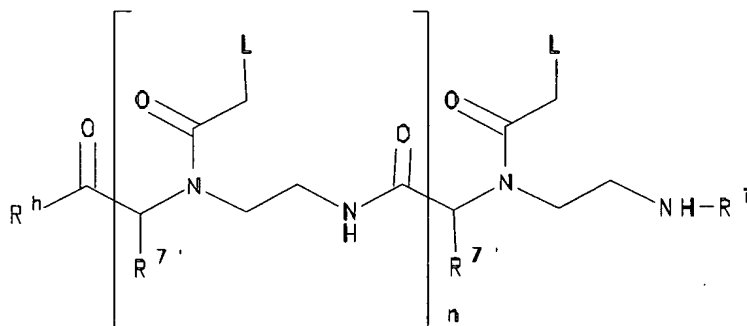
each k and m is, independently, zero or 1;

each l is zero or an integer from 1 to 5;

R<sup>h</sup> is OH, NH<sub>2</sub> or -NHLysNH<sub>2</sub>; and

R<sup>i</sup> is H or COCH<sub>3</sub>.

49. The composition of claim 46 the peptide nucleic acid is of the formula:



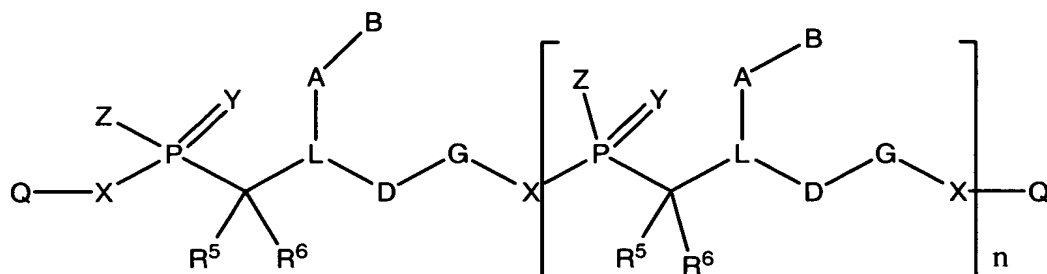
each L is independently selected from the group consisting of the nucleobases

each R<sup>7'</sup> is hydrogen; and

n is an integer from 1 to 30.

50. The composition of claim 49 wherein n is from 20 to about 23.

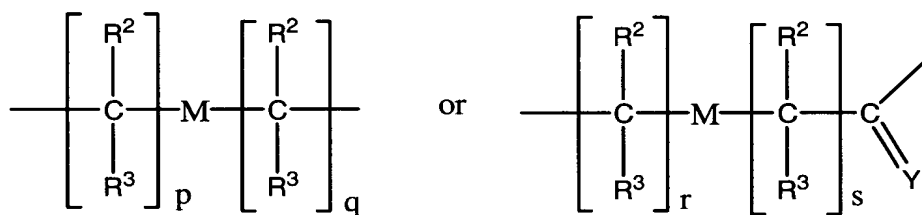
51. The composition of claim 46 wherein the peptide nucleic acid is of the formula:



wherein:

n is a number from zero to 100;

A independently of one another is a single bond, a methylene group or a group of formula



in which M is a single bond, --O--, --S-- or --NR<sup>1</sup>--, where R<sup>1</sup> is hydrogen or (C<sub>1</sub> - C<sub>6</sub>)-alkyl optionally substituted by hydroxyl, (C<sub>1</sub> - C<sub>6</sub>)-alkoxy, (C<sub>1</sub> - C<sub>6</sub>)-alkylthio or amino;

R<sup>2</sup> and R<sup>3</sup> independently of one another are hydrogen, hydroxyl, (C<sub>1</sub> - C<sub>6</sub>)-alkoxy, (C<sub>1</sub> - C<sub>6</sub>)-alkylthio, amino, halogen, or (C<sub>1</sub> - C<sub>6</sub>)-alkyl optionally substituted by hydroxyl, (C<sub>1</sub> - C<sub>6</sub>)-alkoxy or (C<sub>1</sub> - C<sub>6</sub>)-alkylthio;

p and q independently of one another are zero to 5; and

r and s independently of one another are zero to 5;

B independently of one another is hydrogen, hydroxyl, (C<sub>1</sub> - C<sub>20</sub>)-alkyl, (C<sub>1</sub> - C<sub>20</sub>)-alkoxy, (C<sub>1</sub> - C<sub>20</sub>)-alkylthio, (C<sub>6</sub> - C<sub>20</sub>)-aryl-(C<sub>1</sub> - C<sub>6</sub>)-alkyl, (C<sub>6</sub> - C<sub>20</sub>)-aryl-(C<sub>1</sub> - C<sub>6</sub>)-alkoxy, (C<sub>6</sub> - C<sub>20</sub>)-aryl-(C<sub>1</sub> - C<sub>6</sub>)-alkylthio, an aromatic group or a heterocyclic group, wherein the alkyl, alkyl portion of alkoxy or alkylthio, aromatic or heterocyclic group is optionally substituted one or more times by hydroxyl, (C<sub>1</sub> - C<sub>4</sub>)-alkoxy, --NR<sup>9</sup>R<sup>10</sup>, oxo, --C(O)OR<sup>8</sup>, --C(O)NR<sup>9</sup>R<sup>10</sup>, --CN, --F, --Cl, --Br, --NO<sub>2</sub>, (C<sub>2</sub> - C<sub>6</sub>)-alkoxyalkyl, --S(O)<sub>m</sub>R<sup>8</sup>, --(C<sub>1</sub> - C<sub>6</sub>)--alkyl--S(O)<sub>m</sub>R<sup>8</sup>, --

$\text{NHC(=NH)NHR}^8$ ,  $-\text{C(=NH)NHR}^9$ ,  $\text{NR}^9\text{C(=O)R}^8$ ,  $=\text{NOR}^8$ ,  $\text{NR}^9\text{C(=O)OR}^{10}$ ,  $-\text{OC(=O)NR}^9\text{R}^{10}$ ,  $-\text{NR}^9\text{C(=O)NR}^9\text{R}^{10}$ , a natural nucleobase, an unnatural nucleobase or a reporter ligand, with the proviso that at least one B moiety is a nucleobase;

m is zero, 1 or 2; or,

A-B independent of other A and B groups, can be a D- or L-amino acid condensed on via the carboxyl group or a peptide containing amino acids having a length of up to 5 amino acid residues, with the proviso that at least one B moiety is a nucleobase;

L independently of one another is N or  $\text{R}^1\text{N}^+$ , where  $\text{R}^1$  is as defined above; and

$\text{Y}'$  is  $=\text{O}$ ,  $=\text{S}$ ,  $=\text{CH}_2$ ,  $=\text{C}(\text{CH}_3)_2$  or  $=\text{NR}^1$ , where  $\text{R}^1$  is as defined above;

D and G each independently represent  $\text{CR}^5\text{R}^6$  which can be the same or different;

$\text{R}^5$  and  $\text{R}^6$  independently of one another are hydrogen,  $(\text{C}_1-\text{C}_6)$ -alkyl,  $(\text{C}_6-\text{C}_{20})$ -aryl,  $(\text{C}_6-\text{C}_{20})$ -aryl- $(\text{C}_1-\text{C}_6)$ -alkyl, hydroxyl,  $(\text{C}_1-\text{C}_6)$ -alkoxy,  $(\text{C}_1-\text{C}_6)$ -alkylthio, wherein the alkyl, alkyl portion of alkoxy or alkylthio, or aryl group is optionally substituted by  $\text{SR}^1$  or  $\text{NR}^1\text{R}^1$ , where  $\text{R}^1$  is as defined above and  $\text{R}^1$  independently of  $\text{R}^1$  has the same meaning as  $\text{R}^1$ ;

X independently of one another is  $-\text{O}-$ ,  $-\text{S}-$  or  $-\text{NR}^1-$ , in which  $\text{R}^1$  is as defined above;

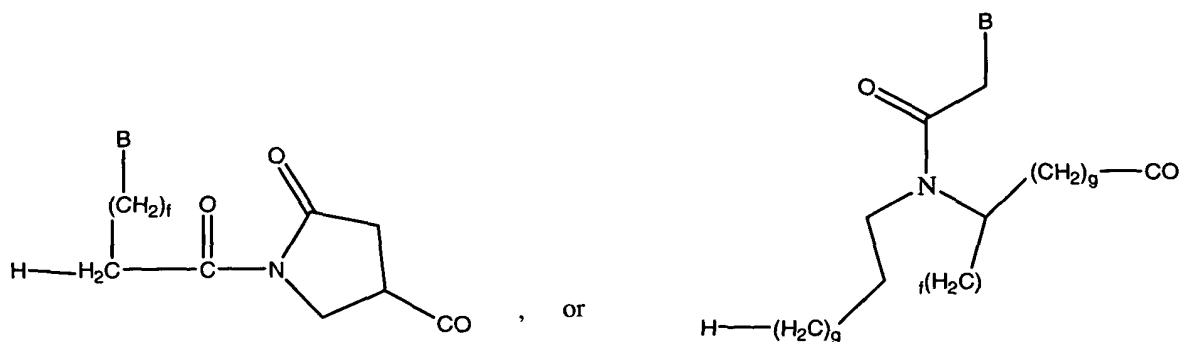
Y independently of one another is  $=\text{O}$  or  $=\text{S}$ ;

Z independently of one another is  $-\text{OR}^8$ ,  $-\text{NR}^9\text{R}^{10}$  or  $\text{X}'\text{Q}''$ , where  $\text{X}'$  is defined as X above and  $\text{Q}''$  is defined as Q below;

$\text{R}^8$  is hydrogen,  $(\text{C}_1-\text{C}_{18})$ -alkyl,  $(\text{C}_2-\text{C}_{18})$ -alkenyl,  $(\text{C}_3-\text{C}_{18})$ -alkynyl,  $(\text{C}_6-\text{C}_{12})$ -aryl,  $(\text{C}_6-\text{C}_{12})$ -aryl- $(\text{C}_1-\text{C}_6)$ -alkyl, wherein alkyl is optionally substituted one or more times by hydroxyl,  $(\text{C}_1-\text{C}_4)$ -alkoxy, F, Cl or Br and wherein aryl is optionally substituted 1-3 times by hydroxyl,  $(\text{C}_1-\text{C}_4)$ -alkoxy,  $(\text{C}_1-\text{C}_4)$ -alkyl, F, Cl, Br,  $\text{NO}_2$ ,  $-\text{NR}^9\text{R}^{10}$ ,  $-\text{C(O)OH}$ ,  $-\text{C(O)O}-$  $(\text{C}_1-\text{C}_6)$ -alkyl or  $-\text{C(O)NR}^9\text{R}^{10}$ ;

$\text{R}^9$  and  $\text{R}^{10}$  independently of one another are hydrogen,  $(\text{C}_1-\text{C}_{18})$ -alkyl,  $(\text{C}_2-\text{C}_{18})$ -alkenyl,  $(\text{C}_3-\text{C}_{18})$ -alkynyl,  $(\text{C}_6-\text{C}_{12})$ -aryl,  $(\text{C}_6-\text{C}_{12})$ -aryl- $(\text{C}_1-\text{C}_6)$ -alkyl, where alkyl is optionally substituted one or more times by hydroxyl,  $(\text{C}_1-\text{C}_4)$ -





where  $l$  is 1-4 and  $g$  is 0-3;  $R^o$  is hydrogen,  $C_1$ - $C_{18}$ -alkanoyl,  $C_1$ - $C_{18}$ -alkoxycarbonyl,  $C_3$ - $C_8$ -cycloalkanoyl,  $C_7$ - $C_{15}$ -aroyl,  $C_3$ - $C_{13}$ -heteroaroyl, or a group which favors intracellular uptake of the oligomer;

A is an amino acid radical;

$k$  is an integer from zero to 10;

Q is an amino acid radical;

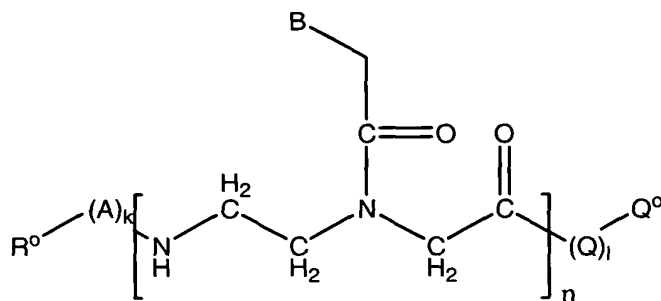
$l$  is an integer from zero to 10;

B is a natural nucleotide base or unnatural nucleotide base conventionally used in nucleotide chemistry or their prodrug forms, or a base substitute compound;

$Q^o$  is hydroxyl,  $NH_2$  or  $NHR''$ , in which  $R''$  is  $C_1$ - $C_{18}$ -alkyl,  $C_2$ - $C_{18}$ -aminoalkyl or  $C_2$ - $C_{18}$ -hydroxyalkyl; and

$n$  is an integer from 1-50.

53. The composition of claim 46 wherein the peptide nucleic acid is of the formula:



where  $R^o$  is hydrogen,  $C_1$ - $C_{18}$ -alkanoyl,  $C_1$ - $C_{18}$ -alkoxycarbonyl,  $C_3$ - $C_8$ -cycloalkanoyl,  $C_7$ - $C_{15}$ -aroyl,  $C_3$ - $C_{13}$ -heteroaroyl, or a group which favors intracellular uptake of the oligomer;

A is an amino acid residue;

k is an integer from zero to 10;

Q is an amino acid residue;

m is an integer from 0 to 20;

B is a nucleotide base;

Q<sup>o</sup> is hydroxyl, NH<sub>2</sub> or NHR'', with R'' is C<sub>1</sub>-C<sub>18</sub>-alkyl, C<sub>2</sub>-C<sub>18</sub>-aminoalkyl or C<sub>2</sub>-C<sub>18</sub>-hydroxyalkyl; and

n is an integer of 1-50.

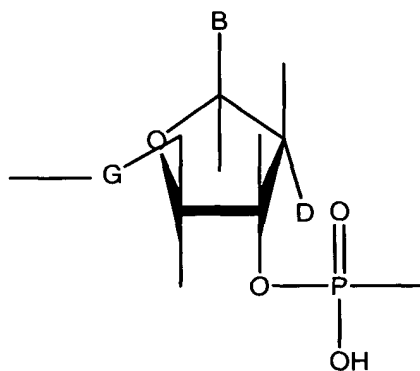
54. The composition of claim 46 wherein the peptide nucleic acid is of the formula:



wherein

Q is a linker or chemical bond;

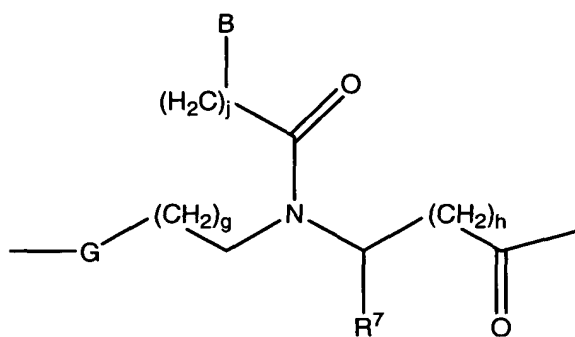
one of L and M is a nucleotide moiety of the formula:



where B is a natural or unnatural nucleobase comprising a bond linking a nucleobase protecting group to the natural or unnatural nucleobase; and

D is a hydrogen atom, a hydroxyl group, a methoxyl group or a hydroxyl group which is protected by a protecting group;

the other of L and M is a PNA moiety of the formula:



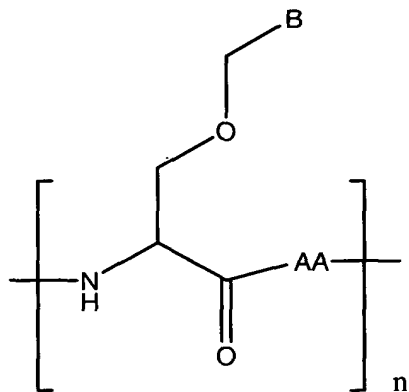
wherein G is a secondary nitrogen atom, a tertiary nitrogen atom having an alkyl substituent, an oxygen atom or a sulfur atom;

B is a natural or unnatural nucleobase;

R<sup>7</sup> is selected from the group consisting of hydrogen and a side chain of a protected or unprotected naturally occurring  $\alpha$ -amino acid; and

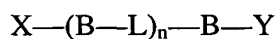
each of j, g and h is the same or different and is independently zero or an integer from one to five.

55. The composition of claim 46 wherein the peptide nucleic acid is of the formula:



where B is a nucleobase, AA is an amino acid, and n is an integer greater than 1.

56. The composition of claim 32 wherein the modification comprises the formula:



where B is a nucleobase capable of effecting Watson/Crick base-pairing and bearing two linking attachment sites;

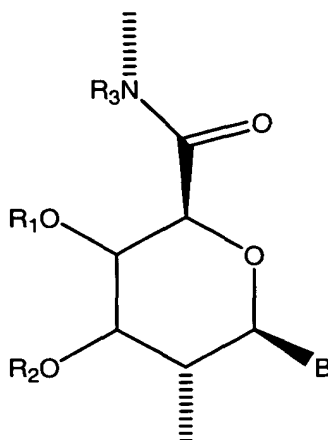
L is a linker comprising 4-7 bonds;

X and Y are terminating groups; and



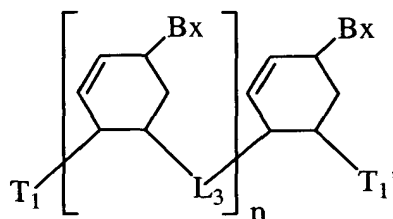
n is an integer equal to 1 or greater.

57. The composition of claim 32 wherein the modification is of formula:



wherein R<sub>1</sub> and R<sub>2</sub> are, independently, hydrogen, lower alkyl or acyl and R<sub>3</sub> is hydrogen or lower alkyl.

58. The composition of claim 32 wherein the modification is of the formula:



wherein

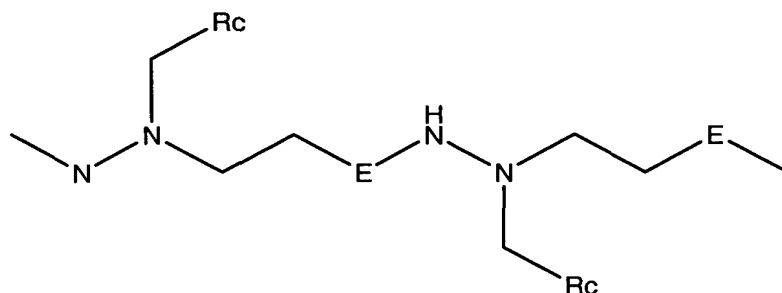
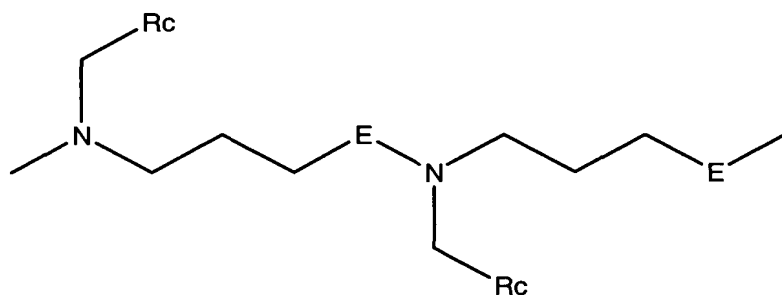
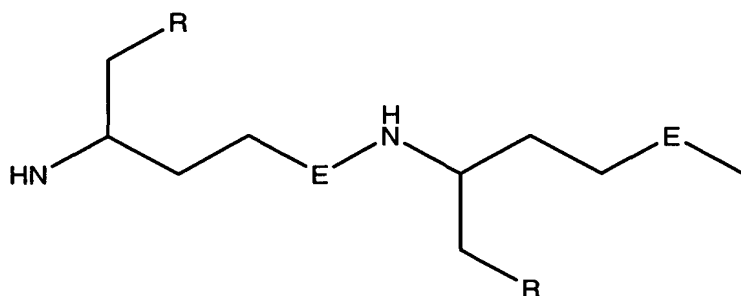
each Bx is a heterocyclic base moiety;

T<sub>1</sub> is hydroxyl or a protected hydroxyl;

T<sub>1</sub>' is hydroxyl or a protected hydroxyl; and

L<sub>3</sub> is an internucleoside linkage.

59. The composition of claim 32 wherein the modification comprises the formula:



where E is C(=O) or SO<sub>2</sub>; and

R and Rc are each independently selected from the group consisting of hydrogen, hydroxy, (C<sub>1</sub>-C<sub>4</sub>)alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, heterocyclic moieties, and reporter ligands, at least one of R and Rc being a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group.

60. The composition of claim 59 wherein at least one R or Rc is a naturally occurring nucleobase, a non-naturally occurring nucleobase.

61. An oligomer having at least a first region and a second region, wherein:

said first region of said oligomer is complementary to and capable of hybridizing with said second region of said oligomer,

at least a portion of said oligomer is complementary to and capable of hybridizing to a selected target nucleic acid, and

said oligomer further includes at least one nucleotide having a modification comprising a peptide nucleic acid, a peptide nucleic acid mimic, a morpholino nucleic acid or an acyclic backbone moiety.

62. The oligomer of claim 61 wherein each of said first and said second regions has at least 10 nucleotides.

63. The oligomer of claim 61 wherein said first regions in a 5' to 3' direction is complementary to said second region in a 3' to 5' direction.

64. The oligomer of claim 61 wherein said oligomer includes a hairpin structure.

65. The oligomer of claim 61 wherein said first region of said oligomer is spaced from said second region of said oligomer by a third region and where said third region comprises at least two nucleotides.

66. The oligomer of claim 61 wherein said first region of said oligomer is spaced from said second region of said oligomer by a third region and where said third region comprises a non-nucleotide region.

67. A pharmaceutical composition comprising the composition of claim 1 and a pharmaceutically acceptable carrier.

68. A pharmaceutical composition comprising the composition of claim 32 and a pharmaceutically acceptable carrier.

69. A pharmaceutical composition comprising the oligomeric compound of claim 61 and a pharmaceutically acceptable carrier.

70. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with a composition of claim 1.

71. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with a composition of claim 32.
72. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with an oligomeric compound of claim 61.
73. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of a composition of claim 1.
74. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of a composition of claim 32.
75. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of a composition of claim 61.